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Implications of median sensory study to the thumb and deltoid/biceps motor unit recruitment on identifying C6 root avulsion in upper neonatal brachial plexus palsy

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Abstract

Introduction/Aims: Anatomic representation suggests that a median sensory nerve conduction study recording the thumb (median D1 NCS) may effectively assess upper neonatal brachial plexus palsy (NBPP). We sought to determine the feasibility of technique, establish reference data, and assess its ability to: (a) identify focal upper plexus lesions; and (b) identify C6 root avulsion. In a secondary analysis, we explored the association between absence/presence of motor unit action potentials (MUAPs) during needle electromyography (EMG) of the deltoid and biceps brachii muscles and C6 avulsion status.

Methods: A retrospective chart review was performed of surgical patients with severe upper NBPP who ultimately underwent surgical reconstruction (between 2017 and 2020). Median D1 sensory nerve action potential (SNAP) amplitude ranges were determined in affected and contralateral limbs and analyzed by C6 root avulsion status. Also, presence/absence of MUAPs during EMG of the deltoid and biceps brachii was compared between C6 avulsion patients and controls.

Results: Thirty-eight patients were included in our analysis. A median D1 NCS study was readily performed, showing a contralateral limb mean amplitude of 27.42 μV (range, 3.8-54.7 μV). Most patients had a low ipsilateral median D1 SNAP amplitude, regardless of C6 avulsion status. Detectable MUAPs in either deltoid or biceps brachii on EMG were atypical in C6 root avulsion.

Discussion: The median D1 NCS identifies upper NBPP, but does not distinguish C6 avulsions from post-ganglionic lesions, likely due to the frequent co-occurrence of post-ganglionic axonal disruption. The presence of MUAPs on deltoid/biceps brachii EMG suggests C6 avulsion is unlikely.

KEYWORDS
brachial plexopathy, electrodiagnosis, median sensory study, neonatal brachial plexus palsy, pediatric nerve conduction studies

Abbreviations: Avg, average; CT, computed tomography; D1, digit 1; D5, digit 5; EDx, electrodiagnosis; EMG, electromyography; MRI, magnetic resonance imaging; MUAP, motor unit action potential; NBPP, neonatal brachial plexus palsy; NCS, nerve conduction study; SNAP, sensory nerve action potential.

1 | INTRODUCTION

Neonatal brachial plexus palsy (NBPP) affects approximately 1 to 2 per 1000 live births,[1] with pathophysiology attributed to perinatal stretch of neural structures.[1] The upper plexus components---C5 and C6 roots and upper trunk---are most frequently involved.[1,2] Neurosurgical reconstruction, typically performed before 12 months of age,[2] can restore function for the 20% to 30% of cases[1] with a poor prognosis for spontaneous recovery.[3] Although assessment of neural function by electrodiagnosis (EDx) is appealing as a tool, a systematic assessment of the prognostic value of EDx in early NBPP showed a paucity of relevant literature, further limited by heterogeneity in study techniques and timing.[2] The role of EDx in NBPP thus remains controversial.[2,4]

Early identification is desirable because root avulsions carry a dismal prognosis for spontaneous recovery. Sensory nerve conduction studies (NCS) are frequently used for this purpose, in lieu of needle electromyography (EMG) of muscles overlying the chest wall, which carries a risk of complication. However, a limitation of sensory NCS in identifying avulsion is that coexistence of post-ganglionic lesions would impair the sensory response and mask a pre-ganglionic lesion. Previous studies have suggested that EDx has relatively high specificity (41.9%-85%) but low sensitivity (27.8%-41.7%) for detection of avulsions in NBPP, with limited sensitivity attributable to frequent presence of combined pre- and post-ganglionic lesions.[2,5]

Limitations in establishing a role for sensory NCS in identification of root avulsions in NBPP have included heterogeneity of sensory NCS used in research studies and limited availability of reference data derived from the contralateral side. Earlier work at this center indicated a sensitivity of EDx of 39.1% and specificity of 96.6% in identifying C6 root avulsions among operative cases of NBPP. In this study, to record the upper and middle portions of the plexus, a combination of digit 1 (thumb), digit 2, and digit 3 median studies was used, and sensory nerve conduction studies were considered abnormal if amplitude was no more than 50% that of the contralateral side or laboratory-based normative limit.

Given that the thumb, or digit 1 (D1), has a greater proportion of axons originating from the C6 root than digit 2 (D2) (reported at 100% for D1 and 20% for D2),[7] we sought to determine the utility of this recording in the assessment of upper NBPP. In adults, the median study recording D1 is more reliable than the D2 recording for detecting upper trunk axon loss[8]; however, reference data for the D1 recording site in infants are lacking. Given limitations of overreliance on normative data comparisons in an age group in which neural structures remain immature,[9] anatomical factors significantly affect NCS parameters,[10] and limited normative data are available,[11] establishment of a diagnostic technique relying on comparison to the contralateral side as an internal reference holds appeal. In this study, we sought to determine whether: (a) a median sensory nerve conduction response recording D1 can be obtained reliably in infants, and to present a range of normative data derived from contralateral limbs; (b) abnormalities of the median D1 response can reliably identify upper brachial plexopathy; and (c) the median D1 study can be used to identify cases of surgically confirmed C6 root avulsion. As a secondary analysis, we collected EMG data to evaluate whether absence vs presence of motor unit action potentials (MUAPs) in deltoid and biceps brachii (both innervated by C6) could predict avulsion.

2 | METHODS

2.1 | Retrospective chart review

This study was conducted in a tertiary referral center specializing in NBPP. The study was reviewed by the institutional review board of the University of Michigan and deemed exempt from ongoing regulation, as secondary research for which consent is not required. Medical records were reviewed for all patients who received surgical intervention (nerve transfers or nerve grafting) between April 2017 and December 2020 for treatment of NBPP who had previously undergone EDx evaluation within the first 10 months of life, with a recorded median D1 SNAP on the affected side (38 cases) and who had a pattern of clinical weakness concerning for a lesion involving the upper brachial plexus (deltoid and/or biceps brachii weakness). Demographic data collected included gender, birthweight, gestational age at birth (both term and preterm infants were included), age at initial neurosurgical consultation and EDx evaluation, and age at surgical intervention. Also noted were the presence of shoulder dystocia at birth, manual muscle testing results in the affected and contralateral limbs at initial consultation, neurogenic findings on EMG (positive sharp waves, fibrillation potentials, decreased MUAP recruitment, or increased MUAP polyphasia, duration or amplitude), and median D1 SNAP amplitudes of the affected and contralateral limbs. The neurosurgeon (L.Y.) reviewed the operative report for each infant to identify cases with C6 root avulsion and controls without C6 avulsion.

2.2 | Electrophysiological techniques

For all patients, an antidromic median D1 NCS was performed, recording with pediatric ring electrodes: active, placed at the base of the first digit, and reference, as distal as possible (not exceeding 3-cm separation). For all pediatric NCS, stimulation sites were based on anatomic landmarks, and distances were measured to calculate conduction velocities. No sedation was used for NCS or EMG.

2.3 | Determination of median D1 SNAP amplitude ranges in contralateral and affected limbs

The range of median D1 SNAP amplitudes of the contralateral limbs was obtained to provide reference median D1 SNAP values in a population with NBPP.

To assess ability of the median D1 SNAP study to identify upper NBPP, the amplitudes of the affected and contralateral sides were compared with a paired *t* test. Unobtainable responses were coded as an amplitude of 0 μV. A reduction of at least 50% in SNAP amplitude compared with the contralateral side was considered abnormal.

In our practice, a contralateral D1 sensory study is sometimes not performed when the ipsilateral D1 SNAP response is low or unobtainable and an ipsilateral ulnar SNAP response recording D5 is normal. As the fifth digit is of similar size to the first digit, we interpret a robust response here as a negative control that can, in conjunction with a low or absent median D1 SNAP, suggest a focal lesion, without need for contralateral studies. For this retrospective review, for patients with an unobtainable median D1 SNAP for whom no contralateral median D1 study was performed, the ipsilateral ulnar D5 SNAP amplitude was verified as normal, and patients' median D1 SNAP amplitude was approximated as 0% of the contralateral side.

2.4 | Characteristics of C6 avulsions and C6 non-avulsions

In the retrospective case-control analysis of C6 root avulsion, cases were defined as patients with surgically confirmed C6 root avulsion by visual inspection; those without surgically identified C6 root avulsion were considered controls. To identify statistical differences in demographic and other variables between C6 avulsion cases and non–C6-avulsed controls, the Mann-Whitney *U* test was used to compare continuous data between these groups (ages, strength in deltoid and biceps brachii, median D1 SNAP amplitude, birthweight) and the Fisher exact test was used to compare binary categorical data (presence of shoulder dystocia, and lack of MUAPs on EMG in both deltoid and biceps brachii).

2.5 | Comparison of median D1 SNAP amplitude in C6 avulsion cases and non–C6-avulsed controls

To determine whether the median D1 SNAP amplitude could distinguish cases of C6 avulsion from non–C6-avulsed controls within the study group of severe upper NBPP, the distributions of the median D1 SNAP amplitudes by absolute value (microvolts), and as percentages of the contralateral (reference) amplitudes, were determined for cases and controls. Patients with no median D1 SNAP response in the affected limb, no contralateral study performed, and normal ipsilateral ulnar D5 SNAP were coded as described previously.

2.6 | MUAP absence in deltoid and biceps brachii as a predictor of avulsion

A secondary analysis explored the potential association of MUAP absence in the C6-innervated deltoid and biceps brachii muscles with C6 root avulsion status. In all patients, both muscles were studied, and MUAP absence was defined as having no MUAPs observed in either muscle. A 2 × 2 contingency table was generated, comparing the characteristic of MUAP absence in both deltoid and biceps brachii among cases of C6 avulsion and non–C6-avulsed controls. Predictive values of MUAP presence and absence for identifying C6 avulsion status were determined.

3 | RESULTS

3.1 | Demographics, physical examination, and electrophysiological characteristics

Medical record review identified 48 patients who had undergone surgical intervention for NBPP. Among these, 10 lacked a preoperative median D1 sensory NCS and were excluded from our study, leaving 38 patients for analysis, all of whom had documented clinical involvement of the upper brachial plexus. The demographic, physical examination, and electrophysiological characteristics of the 38 patients are shown in Table 1. Four preterm infants were included, with the earliest gestational age at birth being 34.1 weeks. The mean age at time of EDx was 12.8 weeks, with a range of 3.6 to 39 weeks. A greater proportion of patients with C6 root avulsion had absent MUAPs in deltoid or biceps brachii on EMG compared with non–C6-avulsed controls (see secondary analysis). The other demographic and physical examination variables did not differ significantly between the two groups.

3.2 | Median D1 SNAP amplitudes in contralateral limbs: Reference data

Figure 1A depicts the ranges of median D1 SNAP amplitudes obtained in affected and contralateral limbs. In all contralateral limbs, the median D1 SNAP was readily obtained, ranging in amplitude from 3.8 to 54.7 μV with an average of 27.4 ± 13.80 μV. Skew (0.12) and kurtosis (−0.33) indicate normal distribution. The amplitude was less than 5 μV in only two patients.

For eight patients in our study population, a contralateral median D1 SNAP amplitude was not performed; in all eight patients, the affected limb median D1 SNAP response was not obtainable (seven patients) or showed very low (1.5 μV) amplitude (one patient), and the ipsilateral D5 ulnar SNAP amplitude was normal (range, 8.7-39.8 μV). Accordingly, Figure 1A shows 30 contralateral limbs and 38 ipsilateral limbs.

3.3 | Median D1 SNAP amplitudes in affected limbs

Median D1 SNAP amplitudes were significantly lower in affected (mean, 4.83 μV; SD, 5.04 μV) compared with contralateral (mean, 27.42 μV; SD, 13.80 μV) limbs, averaging approximately 20% of contralateral amplitudes ($t[29] = -9.648$, $P < .001$, 95% confidence interval [CI] of the difference between means = −27.36 to −17.79; Figure 1A). No affected limb showed a median D1 SNAP amplitude greater than 20 μV.

Figure 1B displays distributions of median D1 SNAP amplitudes depicted as a proportions of the contralateral amplitudes, among cases of C6 root avulsion (dark) as compared with non–C6-avulsed controls (light). The patient with a 1.5-μV ipsilateral response and no contralateral data was excluded from analysis. Regardless of C6

TABLE 1 Demographic, physical examination, and electrophysiological characteristics of patients with neonatal brachial plexus palsy treated surgically

	All patients (N = 38)	Non-avulsion (C6) (n = 30)	Avulsion (C6) (n = 8)	*P* value (non-avulsion vs avulsion)
Male gender	14 (37%)	9 (30%)	5 (63%)	.117
Shoulder dystocia	30 (79%)	22 (73%)	8 (100%)	.164
Birthweight (kg)	3.9 ± 0.6	3.9 ± 0.6	4.2 ± 0.5	.089
Gestational birth age (weeks)	39.1 ± 1.8	39.0 ± 1.9	39.4 ± 1.6	.930
Age at EMG (weeks)	12.8 ± 8.3	13.2 ± 8.3	11.6 ± 8.7	.407
Age at surgery (weeks)	36.9 ± 7.5	37.1 ± 6.9	36.2 ± 10.2	.388
Deltoid strength (1-5)	0.8 ± 1.0	0.9 ± 1.0	0.5 ± 0.9	.297
Biceps brachii strength (1-5)	0.5 ± 0.9	0.6 ± 0.9	0.3 ± 0.8	.470
Absent MUAPs in both deltoid and biceps brachii	14 (37%)	7 (23%)	7 (88%)	.002
Median D1 SNAP affected limb (μV)	3.9 ± 4.9	3.7 ± 5.1	4.5 ± 4.1	.297
Median D1 SNAP contralateral limb (μV)	27.4 ± 13.8	25.6 ± 12.7	32.2 ± 10.4	.158
Median D1 SNAP affected limb as percentage of contralateral limb	19 ± 32%	19 ± 36%	18 ± 16%	.335

Abbreviations: Avg, average; D1, digit 1; EMG, electromyography; MUAP, motor unit action potential; SD, standard deviation; SNAP, sensory nerve action potential.
Note: Data expressed as number (%) or mean ± standard deviation.

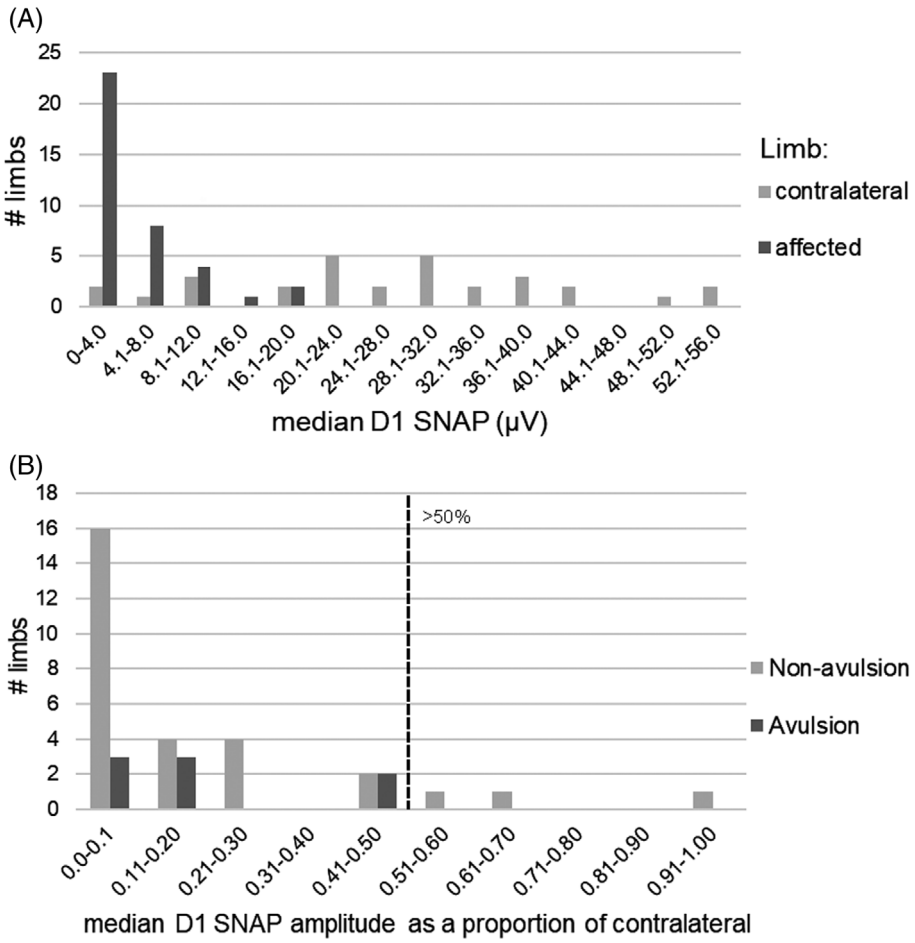

FIGURE 1 A, Distribution of median digit 1 sensory nerve action potential (D1 SNAP) amplitudes among affected (dark; n = 38) and contralateral (light; n = 30) limbs. B, Distribution of affected limb median D1 SNAP amplitudes in proportion to the contralateral amplitudes, in cases of avulsion (dark; n = 8) and non-avulsion (light; n = 29)

TABLE 2 Contingency table illustrating secondary analysis of MUAP presence vs absence among cases of C6 avulsion and non–C6-avulsed controls

Motor units in deltoid/biceps brachii	C6 avulsion (n = 8)	Non–C6 avulsion (n = 30)
Absent	7	7
Present	1	23

Abbreviation: MUAP, motor unit action potential.

avulsion status, most patients (34 of 37) with NBPP in this surgical population showed significant (≥50%) reductions in median D1 SNAP amplitude from the contralateral limb. Although 8 of 37 patients had surgically identified C6 root avulsions, the median D1 study did not identify any, using a threshold of at least 50% amplitude preservation compared with the contralateral side as concerning for avulsion. Of the 29 non–C6-avulsed controls, the median D1 SNAP, if interpreted in isolation from the clinical presentation and EMG, would have falsely identified three avulsions based on the threshold described previously.

3.4 | MUAPs in deltoid/biceps brachii and C6 avulsion status

In our group of 38 patients with surgical upper NBPP, 14 showed no MUAPs in either deltoid or biceps brachii. Table 2 depicts a 2 × 2 contingency table plotting MUAP absence against C6 root avulsion status. In this sample, MUAP absence on EMG in both biceps brachii and deltoid had a positive predictive value of 50% for C6 avulsion. MUAP presence had a 96% predictive value for non-avulsion status at C6. The odds ratio for absent MUAPs in both biceps brachii and deltoid was 23 (95% CI, 2.4-220.33) for C6 avulsion relative to non-avulsion.

Considering dual C5 and C6 innervation to these muscles, C5 root status was also ascertained. There were only three surgically confirmed C5 root avulsions, all of which had concomitant C6 avulsion; among these, two showed no MUAPs in either deltoid or biceps brachii. One additional patient was found to have indeterminate C5 status on intraoperative inspection; this patient did not have C6 avulsion and demonstrated MUAPs in both deltoid and biceps brachii.

4 | DISCUSSION

4.1 | Median D1 sensory NCS can be reliably performed in infants and, when performed bilaterally, may serve as a relevant marker for severe upper brachial plexus palsy

Our small study suggests that severe upper NBPP typically presents with median D1 SNAP amplitudes of less than 20 μV in the affected limb. The median D1 study should be considered when assessing upper brachial plexus palsy, including that of neonatal origin, given D1's greater representation of the relevant axons compared with D2. Given the variability in digit size and neural maturity in infants, a bilateral study is recommended to provide an internal comparison for a unilateral presentation of NBPP.

A limitation of our study is the lack of a strict temperature control, although, in our experience, distal limbs in this age group are typically warm (>30.5°C). Further study is needed to evaluate these findings in larger populations, as well as in populations that include milder clinical phenotypes.

4.2 | Median D1 sensory study does not distinguish root avulsion from post-ganglionic pathology

Our findings align with previous work[6] suggesting limited sensitivity of sensory NCS for avulsion in NBPP, with further elucidation of how this limitation persists even when recording the strongly C6-innervated D1 and using a contralateral internal reference, likely reflecting the presence of combined pre- and post-ganglionic lesions.[12,13] This explanation also aligns with the authors' clinical experience, with our neurosurgical author frequently observing significant neuromatous involvement of the C5 and C6 anterior primary rami and upper trunk in patients with surgically confirmed root avulsion. Potential anatomic, mechanistic, and structural factors that could enhance the degree of combined pre- and post-ganglionic pathology in NBPP, as compared with post-neonatal brachial plexopathy, include longer time in traction, less abrupt nature of traction,[9] increased susceptibility to rootlet injury,[14] different anatomical arrangement of cord and roots,[9] and greater susceptibility to sensory neuronal degeneration.[15] It remains unclear whether combined pre- and post-ganglionic injury occurs more frequently in neonatal than in post-neonatal brachial plexus trauma. Further studies should better explore potential differences between these populations and inform to what degree electrophysiology is expected to differ between post-neonatal and neonatal root avulsion.

4.3 | Presence of MUAPs in either biceps brachii or deltoid is atypical for root avulsion

The high prevalence of MUAP absence in deltoid and biceps likely reflects the severity of pathology in this surgical study population, regardless of pre- vs post-ganglionic localization. That presence of MUAPs in deltoid and biceps strongly predicted lack of avulsion at C6 (96% predictive value) broadly parallels clinical findings using paralysis vs function of biceps brachii as a prognostic indicator that can drive surgical decision-making.[1] Especially when considering that fibrillation potentials and positive sharp waves disappear early in this age group,[4,15] this preliminary finding compels further study of whether, and under what circumstances, presence of MUAPs in deltoid and/or biceps brachii could inform that C6 avulsion is unlikely. Our study

findings suggest that, despite potential contributions from roots beyond C5 and C6 ("luxury innervation"),[4] the identification of any MUAPs is rare in true C6 avulsion. One plausible explanation is a high prevalence of co-occurrence of severe C5 post-ganglionic rupture in these severe cases; indeed, a pattern of C5 post-ganglionic rupture coupled with C6 avulsion has been described in NBPP presenting with clinical deficits in an upper plexus distribution.[16] Our findings do not differentiate whether the absence of deltoid/biceps MUAPs observed in most of the C6 avulsion cases is attributable specifically to the C6 avulsion or to concomitant post-ganglionic lesioning (e.g., upper trunk) in the setting of significant trauma. In practice, our findings suggest that, even within a population of severe NBPP with significant upper limb weakness, assessment of MUAPs on EMG may identify those patients in whom C6 avulsion is unlikely.

4.4 | Study limitations

Several study limitations should be noted. Our study population consisted of severe NBPP cases referred to a tertiary care center, for whom surgical intervention to restore function was offered. Our findings regarding the median D1 study and the presence or absence of MUAPs in deltoid and biceps cannot be applied to patients with mild NBPP. Further studies should address the prognostic role of these features in milder phenotypes, including those in which the clinical diagnosis and appropriate surgical management are in question. In addition, our study did not address surgical outcomes, offer correlation with radiological data, or assess other aspects of EDx (other sensory studies or additional relevant muscles for EMG).

Another limitation is that the EDx study and the decision to offer surgery were not fully independent in this retrospective investigation. It is possible that the EDx consultation influenced: (a) the clinician's decision to offer surgery; and (b) the patient's family's decision to pursue surgery. Our study design is vulnerable to selection bias to the extent that our independent variable (median D1 SNAP amplitude) could have influenced surgical decision-making.

The absence of contralateral median D1 SNAP data in eight patients is also a limitation. Although it cannot be excluded that the contralateral D1 SNAP would have been unobtainable, it is believed to be unlikely based on how reliably this response was obtained, as well as the ability to obtain normal data from another nerve conduction study relying upon a similarly sized digit (fifth digit of hand).

5 | CONCLUSIONS

We found that the median D1 sensory NCS can be performed reliably in infants, and that, when performed bilaterally, it may serve as a relevant marker for severe upper brachial plexus palsy. Our findings build on earlier work[2] cautioning against the use of sensory NCS, in isolation, to identify root avulsions in this group, due to the high co-occurrence of post-ganglionic axonal disruption. However, we found that MUAP presence in either deltoid or biceps brachii was atypical for C6 avulsion. Further research should explore whether this feature can inform clinical prognosis and management.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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